Google

Web Images Groups[New!] News Froogle more »

definition dextrans

Search Advanced Search Preferences

Web

Results 1 - 10 of about 1,930 for definition dextrans. (0.30 seconds)

Tip: Click to get a definition of: dextrans
Or just click on the underlined words in the above colored bar

DEXTRAN - Definition
... Meaning of DEXTRAN. ... **Definition**: A polysaccharide (chain of simple sugars) composed of glucose (a ... When **dextrans** are formed out of sucrose (another type of sugar ...
www.hyperdictionary.com/dictionary/dextran - 5k - Cached - Similar pages

Class Definition
Definition of Class 536. SUBCLASS 51. ... **Dextrans** yield only glucose on hydrolysis but differ otherwise from starch and glycogen as in molecular structure, etc. ...
www.micropat.com/classdef/CLSDEF/class536/s051000.html - 2k - Cached - Similar pages

NDI Terminology - fluorescein dextrans
fluorescein **dextrans**. **DEFINITION**: **Definition** has yet to be entered. Check back later. The definitions used in this glossary of terminology ...
www.ndif.org/Terms/fluorescein_**dextrans**.html - 4k - Cached - Similar pages

Dextrans - Unified Search Environment
... **Definition**: A group of glucose polymers made by certain bacteria. **Dextrans** are used therapeutically as plasma volume expanders and anticoagulants. ...
www.use.hcn.com.au/subject.%60Dextrans%60/home.html - 10k - Cached - Similar pages

Definition of the stimulus to secretion of the nasal salt gland of ...
1970 Jan;2(1):35-7. **Definition** of the stimulus to secretion ... Terms Animals Beak Birds Blood Volume/drug effects Catheterization **Dextrans**/pharmacology Hypertonic ...
www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve& db=PubMed&list_uids=5520749&dopt=Abstract - Similar pages

[PDF] Using Neuronal Tracers
File Format: PDF/Adobe Acrobat - View as HTML
... Most **dextrans** are available as "lysinated", meaning that they have a lysine molecule attached so that they can be easily fixed with aldehyde fixatives and ...
www.hcnr.med.harvard.edu/programs/ R&R/downloads/Using_neuronal_tracers_protocol.pdf - Similar pages

[PPT] www.dcu.ie/~oshead/BE401/lectures/pres41866fc1b02dc.ppt
File Format: Microsoft Powerpoint 97 - View as HTML
... **What is a** Microbial Polysaccharide? ... Structurally **dextrans** are defined today as large class -D-glucans in which -1,6 linkages are predominant. ...
Similar pages

PERMEABILITY OF INTESTINAL CAPILLARIES: Pathway followed by ...
... Good **definition** and high contrast of the tracer particles were obtained in a one ... The glycogens and **dextrans** used move out of the plasma through the fenestrae ...
www.jcb.org/cgi/content/abstract/53/2/365 - Similar pages

www.websters-online-dictionary.org/definition/english/De/Dextrans.html
Similar pages

Class Definition for Class 524 - SYNTHETIC RESINS OR NATURAL ...
... **Dextrans** are a group of compounds differing according to the bacteria used to ... Included within the **definition** of the di- and tri- saccharides are, eg, sucrose ...
www.uspto.gov/go/classification/uspc524/defs524.htm - 101k - Cached - Similar pages

Gooooooooogle ▶
Result Page: 1 2 3 4 5 6 7 8 9 10 **Next**

definition dextrans Search

Search within results | Language Tools | Search Tips | Dissatisfied? Help us improve

Google Home - Advertising Programs - Business Solutions - About Google

Dextrans Topic Tree

Definition:
A group of glucose polymers made by certain bacteria. Dextrans are used therapeutically as plasma volume expanders and anticoagulants. They are also commonly used in biological experimentation and in industry for a wide variety of purposes.

Synonyms and Source Vocabularies:
Dextrans MeSH

Glucans

- **Cellulose**
- **Dextrans**
  - DEAE-Dextran
  - Iron-Dextran Complex
  - Dextran Sulfate
- **Glycogen**
- **Isomaltose**
- **Maltose**
- **Sizofiran**
- **Starch**
- **Trehalose**

Definition of Class 536

SUBCLASS 51

To Parent definition (subclass 18.7) To *Manual* for Class 536

Compounds which are high molecular weight polysaccharides containing D-glucose units linked predominately -D (16).

(1) Note. Dextrans yield only glucose on hydrolysis but differ otherwise from starch and glycogen as in molecular structure, etc.

(2) Note. Dextrans are usually a group of compounds differing according to the bacteria used to ferment the sugar.

(3) Note. Controlled hydrolysis of native dextran yields clinical dextran of lower molecular weight which is useful as a blood plasma substitute.

CLASS 524, SYNTHETIC RESINS OR NATURAL RUBBERS -- PART OF THE CLASS 520 SERIES

Click here for a printable version of this file

SECTION I - CLASS DEFINITION

Class 524 is a continuation of Class 523. Class 523, subclass 1 is the parent subclass of all the Class 524 subclasses.

The Class 523 Class Definition is applicable to both Class 523 and Class 524.

SUBCLASSES

1 **Adding a NRM to a preformed solid polymer or preformed specified intermediate condensation product, composition thereof; or process of treating or composition thereof:**
This subclass is indented under **subclass 1**. Subject matter under Class 523, ... wherein a nonreactant material (NRM) is admixed with a preformed solid polymer (SP) or preformed specified intermediate condensation product (SICP), or the product of such an admixing process.

(1) Note. In many instances wherein a composition is claimed the claims do not indicate the mode of production of the composition. In the absence of such information it is necessary to review the disclosure to determine the mode of preparation of the composition. If it is disclosed that the composition can be prepared by admixing a NRM with a preformed solid polymer or specified intermediate, a notation into this area is required.

(2) Note. This subclass and the indented subclasses hereunder provide for chemical or physical treatments and the products thereof of compositions containing a solid polymer or a preformed specified intermediate composition and a NRM when the claims fails to recite the mode of preparation of the composition and the specification is as noted in the (1) Note, above.

SEE OR SEARCH CLASS:

588, Hazardous or Toxic Waste Destruction or Containment, subclass **255** for polymer or resin containing compositions which contain hazardous or toxic waste to prevent its release into the environment.

2 **Water settable inorganic compound as nonreactive material:**
This subclass is indented under **subclass 1**. Subject matter wherein the added nonreactant material is an inorganic material hardenable by hydration to produce a solid mass, e.g., Portland cement, gypsum cement, etc.

(1) Note. This subclass takes an inorganic material claimed or disclosed by the term "cement" or "setting agent", e.g., aluminum oxide cement, etc.

Degradation of dextrin yields maltose and glucose.

49 **Aldehyde reaction product:**
This subclass is indented under **subclass 47**. Subject matter wherein the starch contains at least two aldehyde groups and is the product generally resulting from the reaction between starch or a derivative thereof and a reactant containing the functional group --OH and derivatives of such compounds.

50 **Ether group, other than solely linking of carbohydrate groups directly to each other:**
This subclass is indented under **subclass 47**. Subject matter wherein the starch has the general formula R-O-R", wherein -R-O is a starch moiety and R" is a carbon atom of a noncarbohydrate containing organic radical and which carbon is not directly bonded to a chalcogen atom by a double bond.

51 **Ester:**
This subclass is indented under **subclass 47**. Subject matter wherein the starch is a compound resulting from the reaction of a hydroxyl group of a starch and an acid.

52 **Solid polymer derived from ethylenic reactants only:**
This subclass is indented under **subclass 47**. Subject matter wherein the carbohydrate is mixed with a solid polymer derived from only ethylenic reactants.

53 **At least one carboxylic acid ester:**
This subclass is indented under **subclass 52**. Subject matter wherein the solid polymer derived from ethylenic reactants only is derived from at least one carboxylic acid ester.

(1) Note. See the Class 520 Glossary wherein the term "carboxylic acid ester" is defined under "carboxylic acid or derivative".

54 **Dextran or derivative:**
This subclass is indented under **subclass 27**. Subject matter wherein the carbohydrate is higher molecular weight polysaccharide containing D-glucose units linked predominately as D (1! 6).

(1) Note. Dextrans yield only glucose on hydrolysis but differ from starch and glycogen as to molecular structure.

(2) Note. Dextrans are a group of compounds differing according to the bacteria used to ferment the sugar.

55 **Gum or derivative:**
This subclass is indented under **subclass 27**. Subject matter wherein the carbohydrate is a highly branched polysaccharide composed of two or more monosaccharides and which are exudations of plants which are produced by the plant to cover wounds and to prevent attack by organisms.

56 **Disaccharide or trisaccharide, e.g., sucrose, etc.:**
This subclass is indented under **subclass 27**. Subject matter wherein the carbohydrate contains only two or three monomeric units each of which contains at least five carbon atoms.

(1) Note. Included within the definition of the di- and tri- saccharides are, e.g., sucrose, lactose, maltose, cellobiose, etc.

57 **Ester:**
This subclass is indented under **subclass 56**. Subject matter wherein the di or trisaccharide is a compound resulting from the reaction of a hydroxyl group of a di or trisaccharide and an acid.

Alginates Topic Tree

Definition:
Salts of alginic acid that are extracted from marine kelp and used to make dental impressions and as absorbent material for surgical dressings.

Synonyms and Source Vocabularies:
Alginates MSH UMLS

Carbohydrates

- **Amino Sugars**
- **Blood Glucose**
- **Deoxy Sugars**
- **Dietary Carbohydrates**
- **Glycoconjugates**
- **Glycosides**
- **Monosaccharides**
- **Polysaccharides**
    - Alginates
    - Carrageenan
    - Chitin
    - Ficoll
    - Fructans
    - Galactans
    - Glucans
    - Glycosaminoglycans
    - Gum Arabic
    - Karaya Gum
    - Lentinan
    - Mannans
    - Oligosaccharides
    - Pectins
    - Pentosan Sulfuric Polyester
    - Polysaccharides, Bacterial
    - Proteoglycans
    - Pyrogens
    - Sepharose
    - Tragacanth
    - Xylans
    - Zymosan
- **Sugar Acids**
- **Sugar Alcohols**
- **Sugar Phosphates**

Google Web Images Groups[New!] News Froogle more »
definition alginates Search Advanced Search Preferences

Web

Results 51 - 60 of about 4,470 for **definition alginates**. (0.08 seconds)

Algae Lecture
... Algae are Thallus, meaning they lack true roots, stems, and leaves, fruits, connecting tissue etc. ... This is like the **alginates** and very valuable. ...
darter.ocps.net/classroom/klenk/Algae.htm - 33k - Cached - Similar pages

HMBV - HMBV - Drying: Continuous drying - Micron flash dryer ...
... Application Food additives such as CMC and **Alginates** are extremely difficult to grind and have a fibrous structure meaning that substantial amounts of energy ...
www.hmbv.nl/english/04_022142_food_additives.asp - 13k - Cached - Similar pages

[PDF] DEFINITION PREVALENCE CAUSES DES ULCERES(1) CAUSES DES ULCERES(2) ...
File Format: PDF/Adobe Acrobat - View as HTML
Page 1. 1 **DEFINITION** ... Charbon Hémorragiques Exsudatives ou ---- Plaies Infectées --- **Alginates** Et/ou ...
www.cicatrisation.info/cours/ulceres.pdf - Similar pages

general information
... In general, though, natural foods meet this **definition**: ... Agar-agar--derived from seaweed. Albumin--derived from egg whites. **Alginates**--derived from seaweed. ...
www.worldwise.com/food.html - 30k - Cached - Similar pages

From Algae to Conifers
... Algae (from the Latin alga, meaning seaweed) have a simple structure not ... The kelp Macrocystis is harvested to provide extracts (**alginates**) that help to give ...
ridge.icu.ac.jp/gen-ed/lower-plants.html - 20k - Cached - Similar pages

WMEP Product 1
... Combinant dressings: **alginates** + hydrocolloid etc. ... The Wound - Field concept encourages the novice or practitioner to examine **what is a** contaminant and what is ...
www.unisa.edu.au/wound/wound_learning_unit.htm - 25k - Cached - Similar pages

Food Additives
... Calcium Alginate - see **Alginates**. ... The FDA **definition** of flavors is as follows: Natural flavor (or natural flavoring) is the essential oil, oleonesic, essence ...
www.kosherquest.org/bookhtml/FOOD_ADDITIVES.htm - 63k - Cached - Similar pages

ific.org : What's This Doing In My Food? A Guide to Food ...
... Gums are classified by source, such as seaweed (which includes agar, **alginates**, carrageenan), plant seed gums (which include guar ... **What is a** GRAS ingredient? ...
www.ific.org/foodinsight/2000/nd/foodingredfi600.cfm - 43k - Cached - Similar pages

[PDF] Microsoft PowerPoint - Products for external application
File Format: PDF/Adobe Acrobat - View as HTML
... Page 19. **Alginates** Salts of alginic acid (E400-405) ... form ribbons similar in appearance to a goat horn (from the Greek "tragos" meaning goat and ...
www.tcd.ie/Pharmaceutics/ Products%20for%20external%20application.pdf - Similar pages

Grafts of microencapsulated pancreatic islet cells for the therapy ...

Systematics of Topicals

1. Liquid Systems
2. Semi-Solid Systems
3. Solid Systems

Hydro-Gels with organic GA's

Natural GA's

- Gelatin (marine!)
- Starch (wallpaper paste)
- Alginate
- Pectin
- Tragacanth

Semi-synthetic GA's

- Cellulose ethers (eg, MC, HEC, HPC, Na-CMC)
- Starch derivatives
- Pectin derivatives

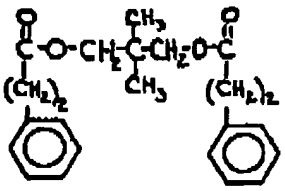
Fully synthetic GA's

- Polyacrylates
- Polyvinyl alcohols (PVA)
- Polyvinylpyrrolidone (PVP)

Alginates

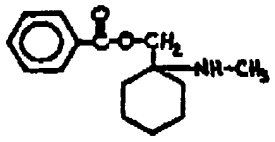
Salts of alginic acid (E400-405)

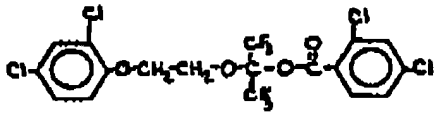
- A mixture of polyuronic acids composed of residues of D-mannuronic acid and L-guluronic acids (Mw ~ 240,000)
- From *Phaeophyceae* (algae)
- Easy soluble in cold water, forms viscous liquids or gels at pH 6-7 (2-10%)
- Sensitive to temperature increase, pH change, salts, but stable ~40% alcohol content



106 **Ring in alcohol moiety:**
This subclass is indented under subclass 103. Compounds wherein the alcohol moiety contains a carbocyclic group.

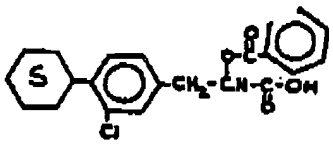
(1) Note. This subclass contains, for example:

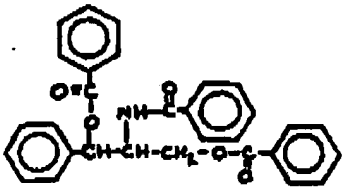




107 **Plural rings in alcohol moiety:**
This subclass is indented under subclass 106. Compounds wherein the alcohol moiety contains more than one carbocyclic group.

(1) Note. This subclass contains, for example:

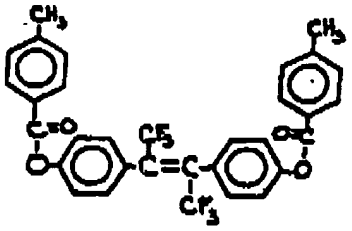


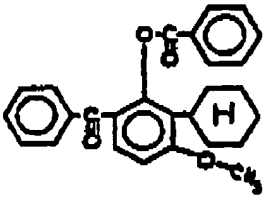


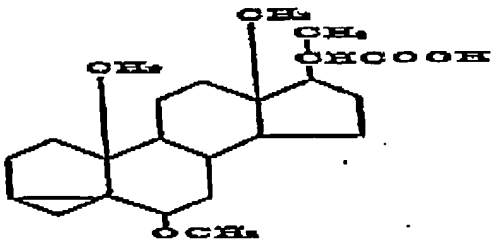
SEE OR SEARCH CLASS:
552, Organic Compounds, subclass 653 for esters of Vitamin D compounds, cholecalciferols, activated 7-dehydrocholesterols, dihydrotachysterols, 3-5 cyclovitamin D compounds, etc.

108 **Esterified phenolic hydroxy:**
This subclass is indented under subclass 107. Compounds wherein the ester function is formed with a phenolic OH group.

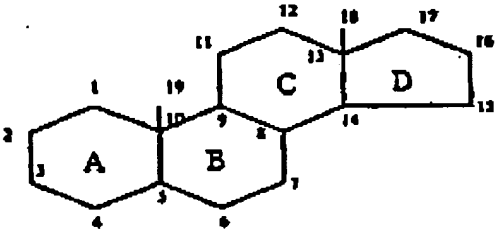
(1) Note. This subclass contains, for example:







P 502 **Cyclopentanohydrophenanthrene ring system containing**
This subclass is indented under subclass 1. Compounds under Class 532, which have the basic structure in Fig. 1 below:



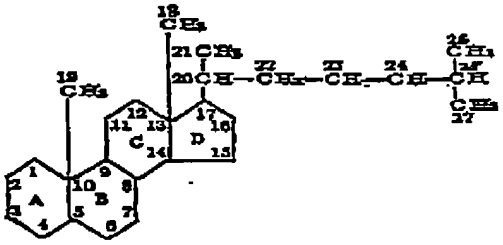
Which may contain double bonds between its ring members.

(1) Note. The phenanthrene portion of this tetracyclic ring system cannot be completely aromatic; it must be hydrogenated to some degree.

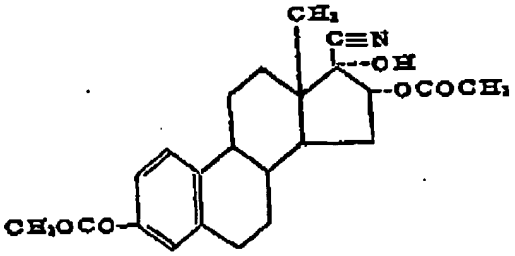
(2) Note. In the indents hereunder which refer to positions, the numbers shown in this definition are employed.

(3) Note. Included herein are compounds which contain an additional ring fused to one or more of the rings of the cyclopentanohydrophenanthrene ring system. See subclasses 510-514.

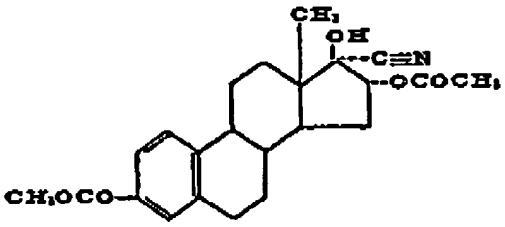
(4) Note. The following structure shows the numbering system for substituents at the 17-position of the cyclopentanohydrophenanthrene ring system:



(5) Note. A substituent at the 17-position of the cyclopentano-hydrophenanthrene ring system is designated as alpha or beta depending upon the stereochemical configuration thereof. A 17 beta-substituent is normally written or drawn directly above the 17-carbon atom and attached thereto by a solid line; a 17-alpha substituent is normally written or drawn to the right of the 17-carbon atom and attached thereto by dotted lines. The drawings below illustrate a cyano substituent as both a 17-beta and 17-alpha substituent.



17B-cyano-3, 16a-diacetoxyestr -1,3,5(10)-trien-17a-ol



17a-cyano-3, 16a-diacetoxyestra-1,3,5,(10)-trien-17B-ol

SEE OR SEARCH THIS CLASS, SUBCLASS:

653, for Vitamin D compounds, calciferols, cholecalciferols, ergocalciferols, activated ergosterols, activated 7-dehydrocholesterols, irradiated ergosterol, irradiated 7-dehydrocholesterol, antirachitic vitamins, dihydrotachysterols, and 3,5-cyclovitamin D compounds.

SEE OR SEARCH CLASS:

514, Drug, Bio-Affecting and Body Treating Compositions, subclasses **169+** for a medicinal composition including a cyclopentanohydrophenanthrene compound.

536, Organic Compounds, subclasses **5+** for sterold glucosides, e.g., digitalis glucosides.

540, Organic Compounds, subclasses **2+** for cyclopentanohydrophenanthrene compounds containing a heterocyclic nucleus.

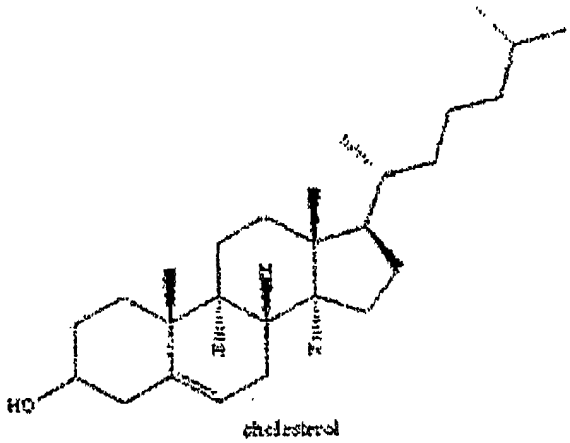
503 **With preservative or stabilizer**
This subclass is indented under subclass 502. Products which contain a compound having a cyclopenthanohydrophenanthrene ring system in admixture with a preserving or stabilizing agent whose sole function is to prevent physical or chemical change.

504 **Heavy metal or aluminum containing**
This subclass is indented under subclass 502. Compounds which include aluminum or a metal having a specific gravity greater than four.

(1) Note. Arsenic is considered a heavy metal.

cholesterol

Cholesterol is a steroid lipid, found in the cell membranes of all body tissues, and transported in the blood plasma, of all animals. Most cholesterol is produced internally, not dietary in origin. It is present in higher concentrations in tissues which either produce more or have more densely packed membranes; for example the liver, spinal cord, brain and atheroma. Cholesterol plays a central role in many biochemical processes, but is best known for the association of cardiovascular disease with various lipoprotein cholesterol transport patterns in the blood.



cholesterol

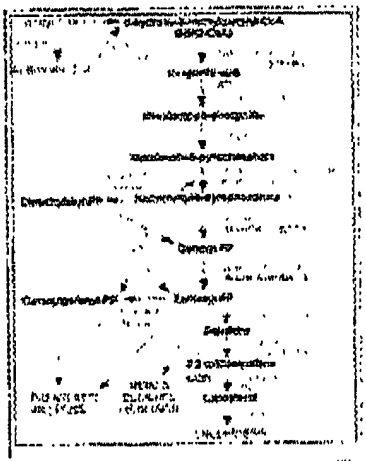
History of the name

The name originates from the Greek *chole-* (bile) and *stereos* (solid), as researchers first identified cholesterol in solid form in gallstones.

Physiology

Synthesis

Cholesterol is primarily synthesized from acetyl CoA through the HMG-CoA reductase pathway in many cells/tissues. About 20–25% of total daily production (~1 g/day) occurs in the liver, other sites of higher synthesis rates include the intestines, adrenal glands and reproductive organs.


The HMG-CoA reductase pathway

Properties

Cholesterol is minimally soluble in water; it cannot dissolve and travel in the water-based blood stream. Instead, it is transported in the blood stream by lipoproteins; protein "molecular-suitcases" which are water soluble and carry cholesterol and fats internally. The proteins forming the surface of the given lipoprotein particle determine from what cells cholesterol will be removed and to where it will be supplied.

The largest lipoproteins, which primarily transport fats from the intestinal mucosa to the liver are called chylomicrons. They carry mostly triglyceride fats and cholesterol (both from food and especially internal cholesterol secreted by the liver into

the bile). In the liver, chylomicron particles give up triglycerides and some cholesterol and are converted into low-density lipoprotein (LDL) particles which carry triglycerides and cholesterol on to other body cells. In healthy individuals the low-density lipoprotein (LDL) particles are large and relatively few in number. Conversely, large numbers of small low-density lipoprotein (LDL) particles are strongly associated with promoting atheromatous disease within the arteries. (Lack of information on low-density lipoprotein (LDL) particle number and size is one of the major problems of conventional lipid tests.)

High-density lipoprotein (HDL) particles transport cholesterol back to the liver for excretion, but vary considerably in their effectiveness for doing this. Having large numbers of large HDL particles correlates with better health outcomes. Conversely, having small amounts of large HDL particles is strongly associated with atheromatous disease progression within the arteries. (Note that the concentration of total HDL does not indicate the actual number of functional large HDL particles, one of the major problems of conventional lipid tests.)

The cholesterol in *LDL cholesterol* and the cholesterol in *HDL cholesterol* are identical. The only difference between the two is the carrier protein molecules (i.e. the lipoprotein).

Regulation

The production is directly regulated by the cholesterol levels present, though the homeostatic mechanisms involved are only partly understood. A higher intake in food leads to a net decrease in endogenous production and *vice versa*. The main regulatory mechanism is the sensing of intracellular cholesterol in the endoplasmic reticulum by the protein SREBP (Sterol Regulatory Element Binding Protein 1 and 2). In the presence of cholesterol, SREBP is bound to two other proteins: SCAP (SREBP-cleavage activating protein) and Insig-1. When cholesterol levels fall, Insig-1 dissociates from the SREBP-SCAP complex, allowing the complex to migrate to the Golgi apparatus, where SREBP is cleaved by S1P and S2P (site 1/2 protease), two enzymes that are activated by SCAP when cholesterol levels are low. The cleaved SREBP then migrates to the nucleus and acts as a transcription factor to bind to the "Sterol Regulatory Element" of a number of genes to stimulate their transcription. Amongst the genes transcribed are the LDL receptor and HMG-CoA reductase. The former scavenges circulating LDL from the bloodstream, while HMG-CoA reductase leads to an increase of endogenous production of cholesterol.

A large part of this mechanism was clarified by Dr Michael S. Brown and Dr Joseph L. Goldstein in the 1970s. They received the Nobel Prize in Physiology or Medicine for their work in 1985.

The average amount of blood cholesterol varies with age, typically rising gradually until one is about 60 years old. A study by Ockrene *et al.* showed that there are seasonal variations in cholesterol levels in humans, more on average in winter.

Function

Cholesterol is an important component of the membranes of cells, providing stability, it makes the membrane's fluidity stable over a bigger temperature interval. The hydroxyl group on cholesterol interacts with the phosphate head of the membrane and the bulky steroid and the hydrocarbon chain is embedded in the membrane. It is the major precursor for the synthesis of vitamin D, of the various steroid hormones, including cortisol, cortisone, and aldosterone in the adrenal glands, and of the sex hormones progesterone, estrogen, and testosterone. Further recent research shows that cholesterol has an important role for the brain synapses as well as in the immune system, including protecting against cancer.

Excretion

Cholesterol is excreted from the liver in bile and reabsorbed from the intestines. Under certain circumstances, when more concentrated, as in the gallbladder, it crystallises and is the major constituent of most gallstones, although lecitin and bilirubin gallstones also occur less frequently.

Role in atheromatous disease

See also the main article hypercholesterolemia

In conditions with elevated concentrations of LDL particles, especially small LDL particles, cholesterol promotes atheroma plaque deposits in the walls of arteries, a condition known as *atherosclerosis*, which is a major contributor to coronary heart disease and other forms of cardiovascular disease. (Conversely, HDL particles have been the only identified mechanism by which cholesterol can be removed from atheroma. Increased concentrations of large HDL particles, not total HDL particles, correlate with lower rates of atheroma progressions, even regression.)

There is a world-wide trend that lower total cholesterol levels tend to correlate with lower atherosclerosis event rates. However, the primary association of atherosclerosis with cholesterol has always been specifically with cholesterol transport patterns, not total cholesterol per se. For example, total cholesterol can be low, yet made up primarily of small LDL and small HDL particles and atheroma growth rates are high. Conversely, if LDL particle number is low (mostly large particles) and a large percentage of the HDL particles are large (HDL is actively reverse transporting cholesterol), then atheroma growth rates are usually low, even negative, for any given total cholesterol concentration.

Multiple human trials using the increasingly more effective combination treatment strategies which have been developed overtime, have repeated confirmed that changing lipoprotein transport patterns from unhealthy to healthier patterns significantly lower cardiovascular disease event rates, even for people with cholesterol values currently considered low for adults. Some of the better recent randomized human outcome trials include ASCOT-LLA, REVERSAL, PROVE-IT, CARDS, Heart Protection Study, HOPE, PROGRESS, COPERNICUS, and especially a newer research approach utilizing a synthetically produced and IV administered human HDL, the Apo A-I Milano Trial.

The American Heart Association provides a set of guidelines for total (fasting) blood cholesterol levels and risk for heart disease:

Level mg/dL	**Level** mmol/L	**Interpretation**
<200	<5.2	Desirable level corresponding to lower risk for heart disease
200-239	5.2-6.2	Borderline high risk
>240	>6.2	High risk

However, as today's testing methods determine LDL ("bad") and HDL ("good") cholesterol separately, this simplistic view has become somewhat outdated. The desirable LDL level is considered to be 75–130 mg/dl (1.9–3.3 mmol/L), and a ratio of total cholesterol to HDL—arguably the most useful measure—of less than 5:1 is thought to be healthy. Patient's should be aware that most testing methods for LDL do not actually measure LDL in their blood, much less particle size. For cost reasons, LDL values have long been estimated using the formula: Total-cholesterol – total-HDL – 20% of the triglyceride value = estimated LDL.

Increasing clinical evidence has strongly supported the greater predictive value of more sophisticated testing which directly measures both LDL and HDL particle concentrations and size as opposed to the more usual estimates/measures of the total cholesterol carried within LDL particles or the total HDL concentration. There are three commercial labs in the United States which offer more sophisticated analysis using different methodologies. As outlined above, the real key is cholesterol transport which is determined by both the proteins which form the lipoprotein particles and the proteins on cell surfaces with which they interact.

Cholesteric liquid crystals

Some cholesterol derivatives, (among others simple cholesteric lipids) are known to generate liquid crystalline phase called "cholesteric". The cholesteric phase is in fact a chiral nematic phase and changes colour when its temperature changes. Therefore cholesterol derivatives are commonly used as temperature sensitive dyes, in liquid crystal thermometers, and in temperature sensitive paints.

See also

- 7-dehydrocholesterol
- triglycerides
- vitamin D

Sources

- Anderson RG. Joe Goldstein and Mike Brown: from cholesterol homeostasis to new paradigms in membrane biology. Trends Cell Biol 2003:13:534-9. PMID 14507481.
- Ockene IS, Chiriboga DE, Stanek EJ 3rd, Harmatz MG, Nicolosi R, Saperia G, Well AD, Freedson P, Merriam PA, Reed G, Ma Y, Matthews CE, Hebert JR. *Seasonal variation in serum cholesterol levels: treatment implications and possible mechanisms.* Arch Intern Med 2004;164:863-70. PMID 15111372.

External links

- Aspects of fat digestion and metabolism - UN/WHO Report 1994
- American Heart Association
- The Weston A. Price Society is a group that questions the connection between cholesterol and atheroma.

The use of synthetic polymers for delivery of DNA

Baubak Bajoghli *

* Matrikelnummer: 9802743, Studienkennzahl: A437, E-mail Adresse: a9802743@unet.univie.ac.at

Abstract:

The safe and efficient delivery of therapeutic DNA to cells represents a fundamental obstacle to the clinical success of gene therapy [1,2]. The challenges facing synthetic delivery vectors are particularly clear, as both cationic polymers and liposomes are less effective at mediating gene transfer than viral vectors. The incorporation of new design criteria has led to recent advances toward functional delivery systems [3,4]. However, the paradigm for the development of polymeric gene delivery vectors remains the incorporation of these designelements into materials as part of an iterative, linear process an effective, albeit slow, approach to the discovery of new vectors [1]. The limitations of viral vectors, in particular their relatively small capacity for therapeutic DNA, safety concerns, difficulty in targeting to specific cell types have led to the evaluation and development of alternative vectors based on synthetic, non-viral systems. The main alternatives to viruses, such as polymers, are described below and include liposomes, liposome-polycation complexes and peptide delivery systems. How the synthesis of this polymers are, is not here discussed but for better describtion of DNA delivery process with Polymers, the use of poly L-Lysin for gene delivery in hepatocyte cells are short explained.

Introduction:

In principle, two basic carrier systems, viral (adeno- and retrovirus) and notviral for DNA delivery in target cells are under development. Viruses are the most wiedly used vectors for systemic delivery of genes, but their efficiency of transfection *in vitro* is not reproduced *in vivo* because of their inherent inflammatory properties, coupled with inappropriate tropisms, which restrict their access to target tissues [5]. Several major problems are associated with the use of viral vectors in clinical treatment. The concept of using block or graft copolymers of cationic and hydrophobic nonionic monomers has been introduced as a potential means for development of nonviral gene delivery vectors [6]. The technical challenge is that DNA (commonly a plasmid) is a particulate material with a net negative charge, a negatively charged surface, and a hydrodynamic diameter of >100 nm. This particle must be introduced into the body and delivered to the target cell across various biological barriers, many of which are normally impeneterable by a particle with these characteristics.

Cationic liposomes and polymers have been accepted as effective non-viral vectors for gene delivery with low immunogenicity unlike viral vectors. The main advantage of using cationic polymers is that polymers carrying different structure elements can be developed by self-assembling with DNA by electrostatic interaction to produce vectors with a range of properties.

The development of self-assembling vectors for DNA delivery is based on synthetic block copolymers. The copolymers will be designed to fulfil a number of biological functions, including condensing the DNA in to discrete particles and stabilising it by enshrouding it

within a hydrophilic polymer coating. An important issue for DNA delivery from polymers is what polymer formulations will give an efficient incorporation and a sustained local delivery in a reproducible manner [12].
In non-viral DNA delivery is important that no single formulation can be used to target all somatic targets. Instead, formulations need to be optimized for each somatic target on the basis of the physiological and biological characteristics of that target.

Liposomal gene delivery:

The structural and phase transformations of lipids are generally inherent to nature and can be applied in practice. Negatively charged, or classical, liposomes have been used to deliver encapsulated drugs for some time and have also been used as vehicles for gene transfer into cells in culture. Problems with the efficiency of nucleic acid encapsulation, coupled with a requirement to separate the DNA-liposome complexes from "ghost" vesicles has lead to the development of positively charged liposomes. Cationic lipids are able to interact spontaneously with negatively charged DNA to form clusters of aggregated vesicles along the nucleic acid. At a critical liposome density the DNA is condensed and becomes encapsulated within a lipid bilayer, although there is also some evidence that cationic liposomes do not actually encapsulate the DNA, but instead bind along the surface of the DNA, maintaining its original size and shape.
Since the cellular membrane is negatively charged, it was the cationic polymers that have received the most attention as potential carriers for DNA how antisense Oligondeoxynucleoic. The coulombic forces governing the interaction betwenn plasma membrane and polycations are so strong that the influence of other properties of the polymers (e.g. hydrophilicity) is drastically diminished. However, the cationic polymers do not constitute the ideal solution for antisense Oligode-oxynucleic [8].

Cationic lipids:

The use of lipids with a polar head group (protonated at physiological pH-cationic) as DNA carriers, poineerede in 1987, has resulted in the commercial production of cell cultur gene-delivery kits and the use of lipopsomal gene delivery in clinical trails. A large number of cationic lipids have been synthesised for gene delivery, some of which are shown in Figure 1. All cationic lipids possess an amine group in addition to hydrophobic group. The amino group binds DNA electrostatically, while the hydrophobic groups facilitate the assembly of cationic lipids into bi-layer vesicles. Lipoplexes (cationic liposome/DNA complexes) range from 50 nm to just over 1 μm in size and an increase in lipoplex size improves transfection *in vitro*. A positively charged lipoplex is necessary for cell binding prior to internalisation by endocytosis. Endosomal escape for onward transport to the nucleus is aided by lipids such 1.2-dioleoyl phosphatidylethanolamine (DOPE).
Cationic lipids have also been shown to be effective agents for DNA transfer *in vivo*. Several different cationic lipids have been used to deliver genes to the lung by intratracheal, intravenous (IV), or intrapul-monary artery routes, resulting in efficient
expression of recombinant genes. Gene delivery with cationic liposomes increases the level of gene expression on IV as the lipoplex prevent plasma degradation of DNA. However, these carriers are severely limited in their applicability via the IV route as they are rapidly cleared from the plasma and gene expression occurs primarily in the lung endothelium, the first capillary bed encountered. Expression is transient, peaking between 4 and 24 hours after dosing and disappearing within a weak.

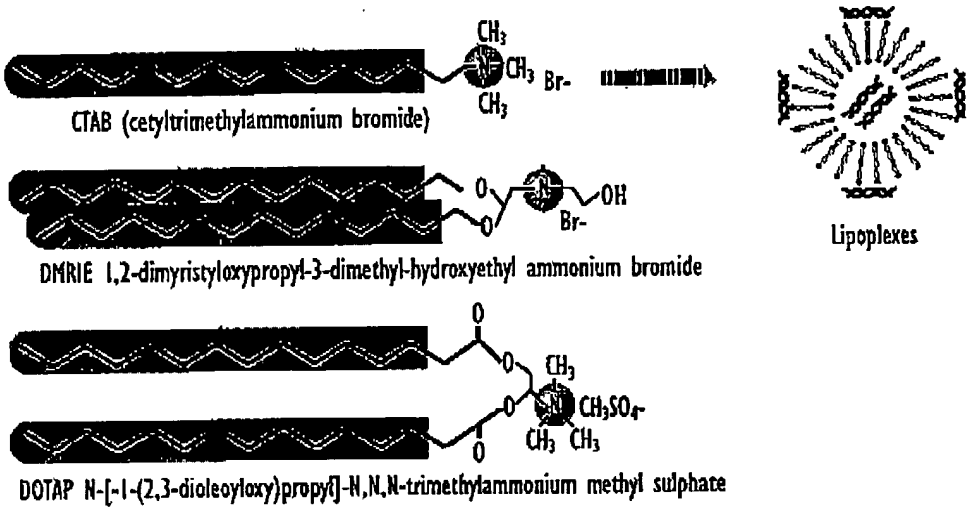


Figure 1: Example of cationic lipids used for DNA delivery

Polymers

Another method for gene delivery utilizes a cationic polymer known as a dendrimer. Dendrimer-DNA complexes are formed by ionic interactions between the positively charged dendrimer and negatively charged DNA. Complexes of different size can be made using dendrimers of different size and different charge ratios. These complexes have been shown to effect efficient gene delivery into a variety of cell types *in vitro* [15].

As with cationic lipids, polymers bearing groups that are protonated at physiological pH have been employed as gene carriers (see Figure 2). The electrostatic attraction between the cationic charge on the polymer and the negatively charged DNA results in a polyplex.

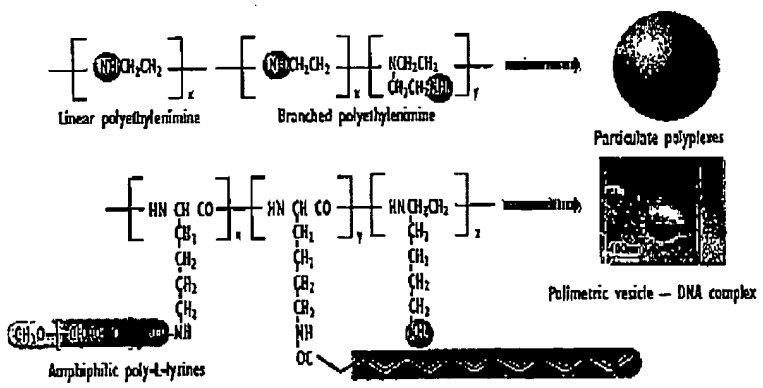


Figure 2: Examples of Cationic Polymers Used for Gene Delivery

Poly L-Lysin (PLL): The use of PLL (Fig 4.a) for gene delivery employs targeting ligands – e.g., asialooroso-mucoid, transferrin and folate, to facilitate receptor – mediated uptake. Without the use of either targeting ligands or lysosomotropic agents (such as chloroquine),

gene transfer is poor with PLL polyplexes alone, an important difference in thebiological activity of the amphiphilic cationic lipids and the soluble polymer PLL. Lipidic PLLs have been prepared and complexed with DNA and the resultant complex was a more efficient transfection agent than cationic liposomes *in vitro*. It appears that amphiphilicity aids gene transfer in some instances. A positively charged polyplex is necessary, presumably to allow interaction with the negatively charged cell surface/endosomolytic uptake, and the incorporation of histidine into PLL polyplexes aids endosomal escape of these agents. A further interesting method of preparing PLL polyplexes involves the replacement of some L-lysine residues with cysteine residues followed by cross-linking to give a superior transfecting unit in which DNA release appears to be triggered by the intracellular reduction of disulphide bonds. Although PLL polyplexes prevent the degradation of DNA by serum nucleases, just like lipoplexes, they are rapidly cleared on IV injection.

From a pharmacokinetic point of view, PLL seems to be a promising hepatocyte-specific carrier; since the hepatotropic nature of cationic polymers is likely due to their positive charge; neutralization of this charge abolishes its affinity for the cells [13]. Complex formation with nucleic acids like plasmid DNA reduces the positive charge of PLL. This, in turn, makes the recognition of glycosylated PLLs via receptors more evident. In addition, the internalization of galactosylated carriers is much faster than that of cationic ones, which could be an advantage for DNA and some drugs [9].

Hepatocyte-specific delivery of DNA was successfully achieved by selecting the most suitable size of PLL and by controlling the galactose density on PLL. If a short PLL with a molecular weight of 1800 is used, a larger amount of PLL is required for complex formation than with PLLs with molecular weights of 13 000 and 29 000. In addition, there is hardly any DNA condensation by the short PLL [13]. To improve the efficiency of galactosylated cationic poly (amino acids)-based gene transfer, the use of compounds that can enhance gene expression such as viruses or viral proteins, fusogenic lipids, and membranedisruptive peptides can be considered. Mitsuru Hashida and his colleagues has suggested that galactosylated polymeric carrier conjugated with a fusogenic peptide was very effective in improving the level of gene transfer after intravenous injection of DNA carrier complexes [17]. Figure 3 gives conceptual explanation about hepatocyte-specific gene delivery with multi-functional polymeric carriers [13].

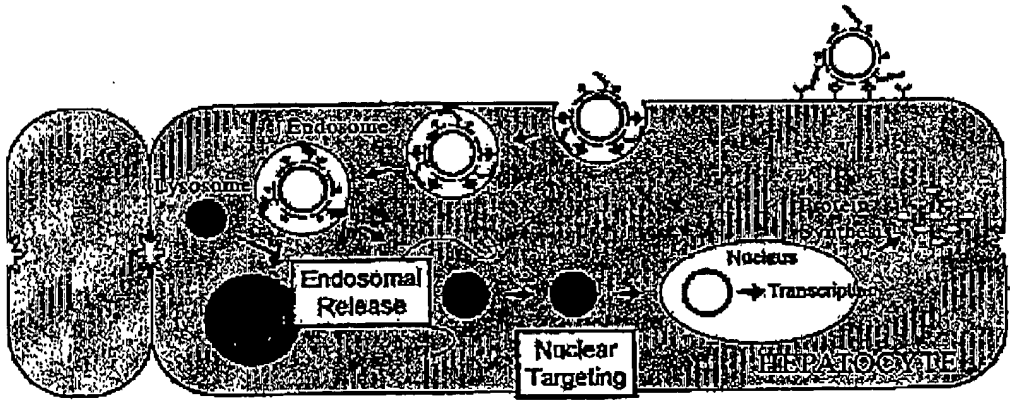


Figure 3: The performance *in vivo* of multifunctional polymeric carriers with galactose moiety for hepatocyte-specific gene delivery [13].

Polyelectrolyte complexes (PECs) are capable of releasing most of the functions mentioned above being, at the same time, suitable for large-scale production. The supramolecular structure of PECs can be described as a hydrophobic core formed by DNA the charge of which was compensated by polycation blocks, surrounded by a shell of hydrophilic polymer chains. So far, several polycations have been used in combination with hydrophilic nonionic polymers to produce complexes with DNA [7].

Polyethylenimine (PEI) is a cationic polymer capable of delivering DNA molecules into cultured mammalian cells as charge complexes (Fig.4.b). The application of PEI polyplexes in gene therapy, however, is hampered by the sensitivity of is transfection activity to the presence of serum.
Both branched and linear PEI shows efficient gene transfer without the need for endosomolytic, lysosomotropic or targeting agents. Linear PEI is more efficient than cationic liposomal formulations *in vivo*. Positively charged PEI polyplexes are endocytosed by cells and PEI is also believed to facilitate endosomal escape. The addition of targeting ligands enhances the activity of PEI presumably by increasing uptake. Recently hydrophobised PEI has been incorporated within DOPE, egg phosphatidylcholine and dipalmitoyl phosphatidylcholine liposomes, producing an efficient gene-transfer agent, although the activity of this soluble amphiphilic polymer was diminished when administered without the liposomal lipids. Unfortunately, PEI, as with some of the cationic lipids, has also been reported to be toxic to cells [14].

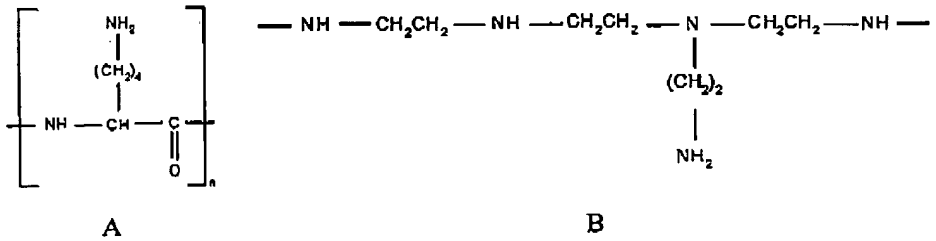


Figure 4: A) Structure of Poly Lysin (PL), B) St ructure of Polyethylenimine (PEI)

Poly (vinylamine) (PVA) was the second type of polycation studied. Molecular weight and dimenstions of DNA complexes formed with PVA were certain degree affected by the molecular weight of the PVA used [4].

Collagen: The first use of polymers to deliver DNA in tissue engineering applications 9 involved the delivery of plasmids encoding for bone morphogenic proteins (BMPs) and fragments of human parathyroid hormone genes. The polymer that used was type I collagen, and the collagen-DNA mixtures were termed gene-activated matrices (GAM)[12].

Liposome/DNA complexe:

There have been several studies on the *in vivo*, systemic use of liposome/DNA complexes. The factors controlling the transfection efficiency of liposome/DNA complexes following IV administration are still poorly understood. The transfection efficiency of liposome/DNA complexes *in vivo* has been shown to be relatively low, especially when compared to viral vectors. One study has suggested that the *in vivo* transfection efficiency of adenoviruses is around 200 times greater than that observed with liposomes. One explanation for the

relatively poor transfection efficiency of liposome/DNA complexes is that they are susceptible to disruption by serum proteins. A variety of proteins are known to bind to liposomes *in vitro* and *in vivo* and may membrane destabilisation. There are now serious efforts being made to develop liposomal vectors that are resistant to serum disruption. Novel cationic lipids are also being developed to try to improve the transfection efficiency of liposome/DNA complexes. Targeting of the liposomes to specific cell types has also been investigated as a means of improving the transfection efficiency.

It was determined that the amount of protein bound to the liposome/DNA complexes is directly proportional to the clearance time of the complexes from the bloodstream. The incorporation of cholesterol into the liposome/DNA formulation, which increases the packing densities of the phospholipid molecules, drastically reduces the amount of bound protein and produces a corresponding improvement in circulation half-life. The incorporation of 30mol % cholesterol increases the half-life of liposome/DNA complexes from seconds to over 5 hours. The amount of serum protein binding to liposome/DNA complexes can also be reduced by increasing the dose of the liposome/DNA complex administered intravenously. This reduction in protein binding produced a corresponding increase in the circulation times, from around 4 minutes to over 80 minutes.

Peptide mediated gene delivery

A related approach is to use naturally occurring or synthetic peptides as gene delivery systems. The interaction of nucleic acids with basic polyelectrolytes is a process that has been known for a long time. In 1946, Kleczkowski showed [10] that the conjugation of proteins with nucleic acids is a general phenomenon that takes place whenever the pH allows them to be of oppisite charges, and also suggested that the interaction of proteins with viral nucleoproteins may be responsible for reducing the infectivity of some viruses.

The importance of serum protein interactions on circulation and transfection activity has been established with cationic liposomes. It is well known that serum has an inhibitory effect on the transfection efficiency of cationic liposome/DNA complexes. Binding of the liposome/DNA complexes to negatively charges serum proteins, leading to a decrease in cell association has been implicated as a mechanism for the inhibitory effect of serum on transfection activity. It has since been demonstrated that this inhibition can, at least partly, be overcome by increasing the charge ratio or dose of the liposome/DNA complex.

The approach of use proteins for DNA delivery is based upon the observation that the functionally active regions of proteins such as enzymes, receptors and antibodies are relatively small, typically consisting of around 10-20 amino acids. Synthesising peptides based upon functional regions of DNA binding proteins or a variety of viral proteins is an approach that has been used to replace the use of whole proteins (such as histone H1) or large, polydispersed polymers (such as polylysine) as gene delivery vectors. A number of peptide sequences have been shown to be able to bind to and condense DNA. One such sequence is the tetra-peptide serine-proline-lysine-lysine located in the C-terminus of the histone H1 protein. Rational design of peptide sequence has also been used to develop completely synthetic DNA binding peptides.

Albumin is another protein that cans interact with DNA complexes by electrostatic or hydrophobic interactions. It has been showed that albumin is not able to decompose the complexes and release free DNA, but it could probably interact with positively charged complexes and form ternary albumin–DNA–polycation complexes. In that case, some parameters of the DNA complexes, such as z-potential or hydrodynamic radius must be changed.

Reference:

[1] David M. Lynn, Daniel G. Anderson, David Putnam, Robert Langer, *Accelerated Discovery of Synthetic Transfection Vectors: Parallel Synthesis and Screening of a Degradable Polymer Library*, J. Am. Chem. Soc., 123(33), (2001) 8155-8156

[2] Luo, D., Saltzman, W. M. Nat. Bio-technol, 18, (2000) 33-37

[3] Lim, Y., Kim, S. et all., J. Am. Chem. Soc. (2001)

[4] Hwang, S. J.; Bellocq, N. C.; Davis, M. E. Bioconjugate Chem. (2001)

[5] A.E.Smith, *viral vectors in gene therapy*, Annu. Rev. Microbila. 49 (1995) 807-838

[6] M.A. Wolfert, Nazarova, L.W. Sey-mour, *Characterization of vectors for gene therapy formed by self-assembly of DNA with synthetic block copolymers*, Hum. Gene Ther. 7 (1996) 2123

[7] D.Oupický, C.Konak, et al., *DNA delivery sytems based on complexes of DNA with synthetic polycations and their copolymers*, Journal of Controlled Release 65 (2000) 149–71

[8] Traian V.Chirila, Ian J.Constable, *The use of synthetic polymers for delivery of therapeutic antisense oligodeoxy-nucleotides*, Biomaterials 23 (2002) 321-42

[9] K. Nishida, H. Sezaki, *Pharmacokinetic analysis of uptake process of lactosaminated albumin in rat liver constant infusion experiments*, Int. J. Pharm. 80 (1992) 101–108.

[10] Kleczkowski, *Combination between different proteins and between proteins and yeast nucleic acid*, Biochem. Journal; 40, (1946) 677-7

[11] Philip R. Dash, Veska Toncheve, L.W. Seymour, *Synthetic polymers for vectorial delivery of DNA: charackteris-ation of polymers-DNA comp-lexes by photon correlation spectroscopy and stability to nuclease degradation and distruption by polyanions in vitro*, J. of Controlled Release 48 (1997) 269-276

[12] Sara-Kaye Madsen and David J. Mooney, *Delivering DNA with polymer matrices: applications in tissue eng-ineering and gene therapy*, PSTT Vol. 3, No. 11 November 2000

[13] Mitsuru Hashida, Yoshinobu Taka-kura, *Cell-specific delivery of genes with glycosylated carriers*, Advanced Drug Delivery Reviews 52 (2001) 187–196

[14] Haeshin Lee, Ji Hoon Jeong, Tae Gwan Park, *A new gene delivery formulation of polyethylenimine / DNA complexes coated with PEG conjugated fusogenic peptide*, Journal of Controlled Release 76 (2001) 183–192

[15] Haensler J, Szoka FC Jr, *Polyamido-amine cascade polymers mediate efficient transfection of cells in culture*. Bioconjug Chem (1993), 4: 372-379

[16] Fred D Ledley, *Non-viral gene therapy*, Current Opinion in Biotechnology (1994) 5: 626-636

[17] M. Nishikawa, M. Yamauchi, K. Morimoto, E. Ishida, Y. Takakura, M. Hashida, *Hepatocyte-targeted in vivo gene expression by intravenous injection of plasmid DNA com- plexed with synthetic multifunctional gene delivery system*, Gene Ther. 7 (2000) 548